Remarks / Arguments

As a result of this amendment, claims 1-5 are pending in the application. Claims 1-4 have been amended. No new matter has been added.

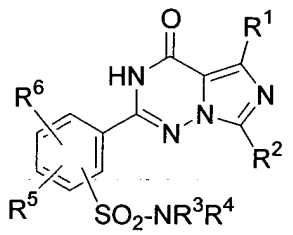
Claim Rejections - 35 USC § 112

Claims 1-5 have been rejected under 35 USC § 112, second paragraph as being indefinite by citing the term "if appropriate". The term "if appropriate" has been replaced by the term "optionally" in claims 1-4 where appropriate. As a result of this amendment, claim 5 is dependent on an allowable base claim and therefore also allowable.

Claim Rejections - 35 USC § 103

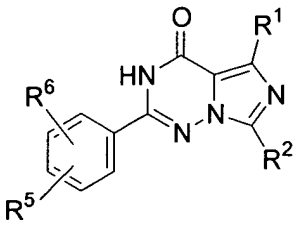
Claims 1-5 have been rejected under 35 USC § 103 as being unpatentable over Niewoehner et al. in view of Dale et al. and Knaggs et al.

The present invention relates to a process for the preparation of compounds of the formula (I)



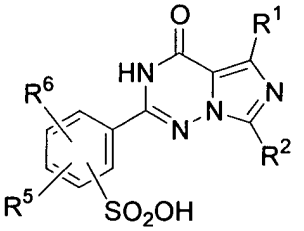
(I),

characterized in that compounds of the formula (II)



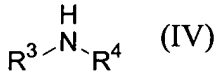
(II),

are reacted with sulphuric acid to give compounds of the formula (III)



(III),

and then with thionyl chloride and the product thus obtained is reacted in situ in an inert solvent with an amine of the formula (IV)



(IV)

Niewoehner et al. discloses a process for chlorosulfonation of aromatic compounds (IV) as shown on pages 54 and 55 with chlorosulfonic acid to sulfonyl chloride compounds (V) and subsequent reaction with amines (VI) to compounds (I).

Dale et al. discloses a process for sulfonation of 2-ethoxybenzoic acid with chlorosulfonic acid and thionyl chloride to the sulfonyl chloride (9), as shown on page 19, which is treated with water, isolated and subsequently reacted with N-methylpiperazine to compound (8).

Knaggs et al. discloses a process for sulfonation of aromatic compounds with sulfonic acid.

None of the above references teaches or suggests the sulfonation of compounds (II) with sulfonic acid to sulfonic acid compounds (III), followed by reaction with thionyl chloride and *in situ* reaction with amines (IV) to compounds (I).

As described in Dale et al. (page 17, column 2), sulfonyl chlorides are potentially toxic materials. None of the above references teaches or suggests the *in situ* reaction of sulfonic acid compounds with thionyl chloride and amines to sulfonyl amides, thereby eliminating one step of isolating a potentially toxic product.

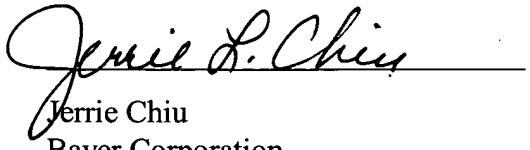
Furthermore, the process of the present invention offers the advantage of recovering the unreacted thionyl chloride by destillation out of the reaction vessel (see example 1.b). Thionyl chloride is a corrosive and cancer suspect agent; the process of the present invention can reduce its handling and transporting steps and provide for its better utilization. On the contrary, when following the process disclosed by Dale et al., the thionyl chloride must be hydrolyzed upon work-up of the chlorosulfonation step and thus cannot be recovered.

As a result of this amendment, claims 1-4 are allowable. Claim 5 is allowable because it is dependent on an allowable base claim.

Conclusion

Applicants respectfully submit that the pending claims are in condition for allowance. Reconsideration is respectfully requested. Please charge any fees due with this amendment to deposit account number 13-3372. If the Examiner believes that a conversation with Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned attorney at (203) 812-3964.

Respectfully submitted,

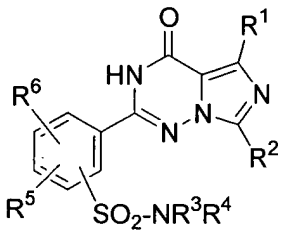


Reg. No. 41,670
Phone: (203) 812-3964
Date: NOV 13 2002

Jerrie Chiu
Bayer Corporation
400 Morgan Lane
West Haven, CT 06516-4175

Version with Markings to Show Changes Made

1. (Amended) Process for the preparation of compounds of the formula I



(I),

in which

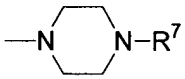
R^1 represents hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms,

R^2 represents straight-chain or branched alkyl having up to 4 carbon atoms,

R^3 and R^4 are identical or different and represent a straight chain or branched alkyl chain having up to 5 carbon atoms, which is optionally substituted up to two times in an identical or different manner by hydroxyl or methoxy,

or

R^3 and R^4, together with the nitrogen atom, form a piperidinyl, morpholinyl or thiomorpholinyl ring or a radical of the formula



in which

R^7 denotes hydrogen, formyl, straight-chain or branched acyl or alkoxycarbonyl each having up to 6 carbon atoms, or straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally mono- to disubstituted, in an identical or different manner, by hydroxyl, carboxyl, straight-chain or branched alkoxy or alkoxycarbonyl each having up to 6 carbon atoms, or denotes C_{3-8} -cycloalkyl,

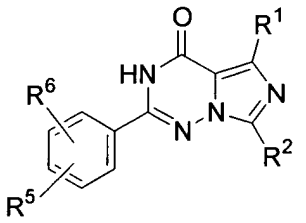
and the heterocycles mentioned under R^3 and R^4, formed together with the nitrogen atom, are optionally mono-to disubstituted, in an identical or different manner, optionally [, if appropriate,] also geminally, by hydroxyl, formyl, carboxyl, straight-chain or branched acyl or alkoxycarbonyl each having up to 6 carbon atoms,

and/or the heterocycycles mentioned under R^3 and R^4, formed together with the nitrogen atom, are optionally substituted by straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally mono- to disubstituted, in an identical or different manner, by hydroxyl or carboxyl,

and/or the heterocycles mentioned under R^3 and R^4, formed together with the nitrogen atom, are optionally substituted by piperidinyl or pyrrolidinyl linked via N,

R^5 and R^6 are identical or different and represent hydrogen, straight-chain or branched alkyl having up to 6 carbon atoms, hydroxyl or straight-chain or branched alkoxy having up to 6 carbon atoms,

characterized in that compounds of the formula (II)

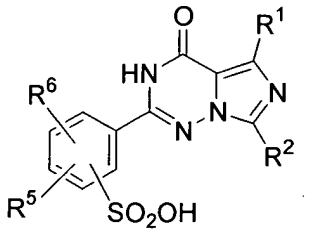


(II),

in which

R^1, R^2, R^5 and R^6 have the meanings indicated above,

are reacted with sulphuric acid to give compounds of the formula (III)

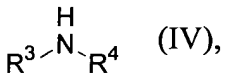


(III),

in which

R^1, R^2, R^5 and R^6 have the meanings indicated above,

and then with thionyl chloride and the product thus obtained is reacted in situ in an inert solvent with an amine of the formula (IV)



(IV),

in which

R^3 and R^4 have the meaning indicated above,

and optionally [, if appropriate,] reacted to give the corresponding salts, hydrates or N-oxides.

2. Process according to Claim 1, characterized in that

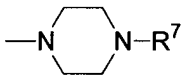
R^1 denotes hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms,

R^2 denotes straight-chain alkyl having up to 4 carbon atoms,

R^3 and R^4 identically to or differently from one another denote a straight-chain or branched alkyl chain having up to 5 carbon atoms, which is optionally substituted up to two times in an identical or different manner by hydroxyl or methoxy,

or

R^3 and R^4, together with the nitrogen atom, form a piperidinyl or morpholinyl ring or a radical of the formula



in which

R^7 denotes hydrogen, straight-chain or branched alkyl having up to 4 carbon atoms, which is optionally mono- or disubstituted, in an identical or different manner, by hydroxyl, straight-chain or branched alkoxy each having up to 4 carbon atoms, or denotes C_{3-6}–cycloalkyl,

and the heterocycles mentioned under R^3 and R^4, formed together with the nitrogen atom, are optionally mono- or disubstituted, in an identical or different manner, optionally [, if appropriate,] also geminally, by hydroxyl, straight-chain or branched acyl or alkoxycarbonyl each having

up to 4 carbon atoms, which is optionally mono- or disubstituted, in an identical or diffferent manner, by hydroxyl,

R^5 and R^6 identically to or differently from one another denote hydrogen, straight-chain or branched alkyl having up to 6 carbon atoms, hydroxyl or straight-chain or branched alkoxy having up to 6 carbon atoms.

3. Process according to Claim 1, characterized in that

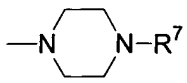
R^1 denotes hydrogen or straight chain or branched alkyl having up to 4 carbon atoms,

R^2 denotes straight-chain alkyl having up to 4 carbon atoms,

R^3 and R^4 identically to or differently from one another denote methyl or ethyl, which are optionally substituted up to two times in an identical or different manner by hydroxyl,

or

R^3 and R^4, together with the nitrogen atom, form a piperidinyl or morpholinyl ring or a radical of the formula



in which

R^7 denotes hydrogen, methyl or ethyl, which is optionally mono-or disubstituted, in an identical or different manner, by hydroxyl, methoxy or ethoxy, or denotes cyclopentyl or cyclohexyl,

and the heterocycles mentioned under R^3 and R^4, formed together with the nitrogen atom, are optionally mono-or disubstituted, in an identical or different manner, optionally [, if appropriate,] also geminally, by hydroxyl, methyl or ethyl,

R^5 and R^6 identically to or differently from one another denote hydrogen, straight-chain or branched alkyl having up to 6 carbon atoms, hydroxyl or straight-chain or branched alkoxy having up to 6 carbon atoms.

4. Process according to Claim 1, characterized in that

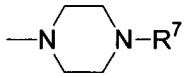
R^1 denotes methyl or ethyl,

R^2 denotes n-propyl,

R^3 and R^4 identically to or differently from one another denote methyl or ethyl, which are optionally substituted up to two times in an identical or different manner by hydroxyl,

or

R^3 and R^4, together with the nitrogen atom, form a piperidinyl or morpholinyl ring or a radical of the formula



in which

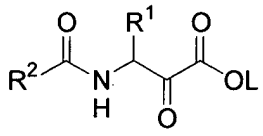
R^7 denotes hydrogen, methyl or ethyl, which is optionally mono- or disubstituted, in an identical or different manner, by hydroxyl, methoxy or ethoxy, or denotes cyclopentyl or cyclohexyl,

and the heterocycles mentioned under R^3 and R^4, formed together with the nitrogen atom, are optionally mono- or disubstituted, in an identical or different manner, optionally [, if appropriate,] also geminally, by hydroxyl, methyl or ethyl,

R^5 denotes hydrogen,

R^6 denotes ethoxy.

5. Process according to Claim 1, characterized in that the compounds of the formula (II) are prepared by reaction of the compounds of the formula (V)



(V),

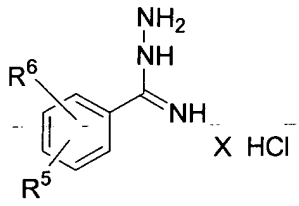
in which

R^1 and R^2 have the meaning indicated Claim 1

and

L represents straight-chain or branched alkyl having up to 4 carbon atoms,

with compounds of the general formula (VI)



(VI),

in which

R^5 and R^6 have the meaning indicated in Claim 1

in a two-stage reaction in the systems methanol and phosphorous oxychloride / acetic acid or methanol and acetyl chloride / acetic acid.